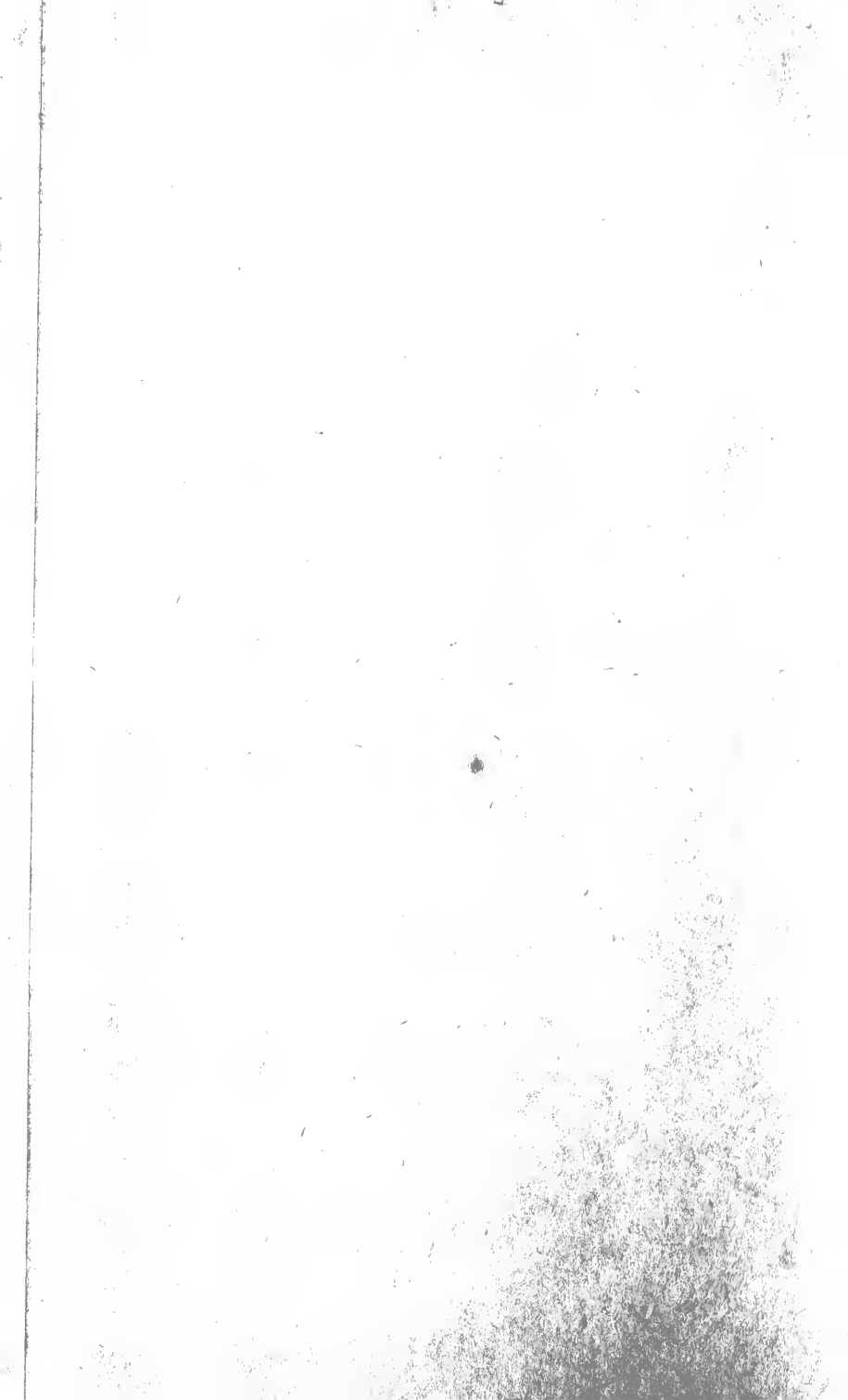


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ON THE
COAGULATION OF THE BLOOD.

THE CROONIAN LECTURE

DELIVERED BEFORE THE ROYAL SOCIETY OF LONDON

11TH JUNE 1863.

BY

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[*From the* PROCEEDINGS *of the* ROYAL SOCIETY.]

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THE subject on which I have the honour to address you this evening, is one which lies at the foundation both of Physiology and Pathology, and, on account of its great importance, has engaged the best energies of many very able men, among whom may be mentioned, for example, such distinguished Fellows of this Society as John Hunter and Hewson ; so that it might well seem presumptuous in me to hope to communicate anything new regarding it, were it not that the constant progress of Physiology and the allied sciences is ever opening up fresh paths for inquiry, and ever affording fresh facilities for pursuing them. Indeed, my difficulty, on the present occasion, does not depend so much on the lack of materials as on the complicated relations of the subject, which make me almost despair of being able, in the short time that can be devoted to a lecture, to give, in anything like an intelligible form, even an adequate selection of the facts at my disposal.

It may, in the first place, be worth while, more especially for the sake of any present who may not be physiologists, to mention very briefly some well-known general facts respecting the constitution of the blood. The blood, if examined by the microscope within the vessels of a living animal, is seen to consist of a liquid and numerous small particles suspended in it. The liquid is termed the "*liquor sanguinis*," the particles the "*blood-corpuscles*." Of these corpuscles a few are colourless, and are named the "*colourless*" or "*white corpuscles*." The great majority are coloured and cause the red appearance of the blood, and hence are called the "*red corpuscles*." Soon after blood has been shed from the body, it passes from the fluid into the solid form. This depends upon the development in the blood of a solid material termed "*fibrin*," so called from its fibrous nature, consisting, as examined by the naked eye, of tenacious fibres, and having the same character also under the microscope. These fibres form a complicated network among the blood-corpuscles, and from their tenacity are the cause of the firmness of the clot. Soon after the process of solidification or coagulation is complete, the fibrin exhibits a disposition to shrink, and squeezes out from among the corpuscles entangled in its meshes a straw-coloured fluid termed the serum, very rich in albumen, in fact very

similar in chemical composition to the fibrin, which, in its turn, may be said to be identical chemically with the material of muscular fibre.

The question before us, therefore, is, What is the cause of the development of this solid material, the fibrin? The subject may be looked at in two aspects,—first, as to the essential nature of the process of coagulation; and secondly, as to the cause of its occurrence when the blood is removed from the body.

With regard to the first point, the essential nature of the process of coagulation, different views have been entertained. John Hunter was of opinion that the coagulation of the blood, the solidification of the fibrin, was an act of life—analogous, in some respects, to the contraction of muscular fibre. This, on the other hand, was made very unlikely by the observation of his contemporary, Mr. Hewson, that blood may be kept in the fluid state by the addition of various neutral salts, but retains the faculty of coagulating when water is added to the mixture. Mr. Gulliver, on one occasion, kept blood fluid, by means of nitre, for upwards of a year, but found that it still coagulated on the addition of water. It seems exceedingly improbable that any part of the human body should retain its vital properties after being thus pickled for more than a year. But here I would wish to make an explanation of the use of this term “vital properties.” When employing it, I do not wish to commit myself to any particular theory of the nature of life, or even to the belief that the actions of living bodies are not all conducted in obedience to physical and chemical laws. But it appears that every component tissue of the human body has its own life, its own health, just as we ourselves have; and as the actions of living men will ever retain their interest whatever views be entertained of the nature of life, so must the actions of the living tissues ever continue to be essential objects of study to the physiologist and pathologist. When, therefore, I use the term “vital properties,” I mean simply properties peculiar to the tissues as components of the healthy living body.

Turning now to the other aspect of the subject of coagulation—the cause of the occurrence of that process on the escape of the blood from the living body—we find that here again various theories have been held, which may be divided into mechanical, chemical, and vital. The mechanical theory was, that mere rest of the blood was sufficient to cause coagulation. I say this *was* the theory; but I

believe it will be found to be still taught by many, that the cause of the coagulation of the blood in an artery which has been tied is its stagnation in the vicinity of the ligature.

As to the chemical theories they have been various. One very natural view was, that exposure to the air was the essential cause of coagulation. Mr. Hewson believed that this was, at all events, an important element in the causes of the phenomenon; and many eminent physiologists and pathologists have held the same view, except that, instead of the air as a whole, the oxygen of the air has been supposed to be the important element.

Sir Charles Scudamore considered that coagulation was greatly promoted by the escape of carbonic acid; and more recently the evolution of ammonia has been regarded as the essential cause of the change. According to the ammonia theory, due to Dr. Richardson of this city, the fluidity of the blood within the body depends on a certain amount of free ammonia holding the fibrin in solution, and the coagulation of the blood when withdrawn from the vessels is the result of the escape of the volatile alkali.

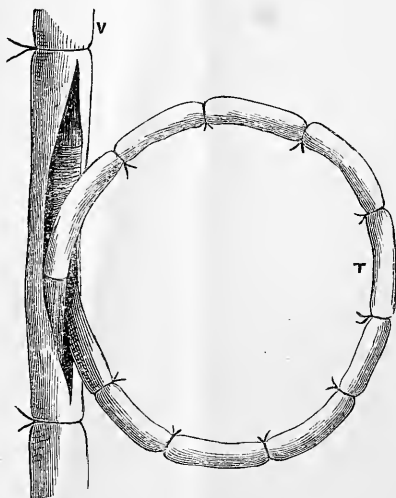
Then, as to vital theories. These have been held by many physiologists, among whom may be mentioned Sir Astley Cooper and Mr. Thackrah, who, from experiments which they performed, were led to the inference that the living vessels exert an active influence upon the blood, by which coagulation is prevented; and Mr. Thackrah went so far as to attribute this action of the vessels to nervous influence. The view that the blood is kept fluid by the operation of its natural receptacles has been advocated more recently by Brücke of Vienna, whose essay will be found in the 'British and Foreign Medical Review' for 1857. Brücke performed his experiments on turtles and frogs, in which animals the blood remains fluid in the heart for days after death; and I feel bound to say that some of the facts which he has brought forward seem to me quite sufficient to show that the ammonia theory, whatever amount of truth it may contain, cannot be the whole truth, and cannot explain the fluidity of the blood within the body. For example, Brücke found that, having shed blood from the heart of a living turtle into a basin, and transferred, with a syringe, a portion of that blood into the empty heart of another turtle just killed, the blood thus transferred into the empty heart remained fluid for hours; whereas that which was left in the basin coagulated in a few minutes. He also found

that blood continued fluid in the heart of a turtle long after the injection of air into the heart through a vein till the cavities of the organ contained a foamy mixture of blood and air.

Yet it by no means follows that the vital theory and the ammonia theory are necessarily altogether inconsistent. It might be true for anything we could tell, *à priori*, that the coagulation of the blood, when shed from the body, might depend on the evolution of a certain amount of ammonia, previously holding the fibrin in solution, and yet it might, at the same time, be true that the cause of the ammonia remaining in the blood in the healthy vessels might be an action of the living vessels retaining it there. It might be that an action of the living vessels might chain down the ammonia and prevent it from escaping, whereas, when shed from the body, it would be free to escape.

This notion was, I confess, at one time entertained by myself; and one of my earliest experiments was performed with a view to the corroboration of the ammonia theory as applied to blood outside the body. It seemed to me desirable that further evidence should be afforded of the effect of mere occlusion from air in maintaining the

Fig. 1.



blood fluid. If the ammonia theory were true, then if blood could be shed directly from a living vessel into an air-tight receptacle composed

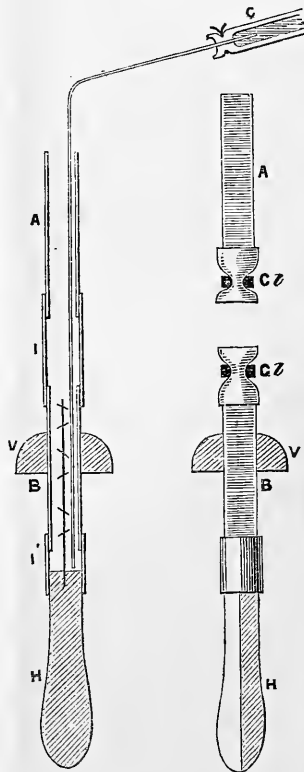
of ordinary matter it ought to remain fluid. For this purpose, I made the following experiment :—I tied into the jugular vein, V, (fig. 1) of a sheep a long vulcanized india-rubber tube, T, adapted by means of short pieces of glass tube at its extremities, both ends being connected with the vessel so that the current of blood might be permitted to flow through the tube, and then continue its natural course. When it had been ascertained that the blood was circulating freely through the tube, which could be readily done by placing the finger on the cardiac aspect of the vein, which was then made to swell if the circulation was proceeding through the tube, pieces of string well-waxed were tied at intervals of about 2 inches round the tube, which was thus converted into a number of air-tight receptacles containing blood, which certainly had no opportunity for the escape of ammonia. The tube was then removed, and I found, in accordance with the view which I was then disposed to entertain, that the blood, instead of coagulating completely in a few minutes as it would have done if shed into a cup, remained partially fluid in these receptacles after the lapse of three hours. But I have since found that if the experiment be repeated in the same way as regards its earlier stages, and if, after a few of the strings have been tied on, the tube be cut across, the blood which is in the part of the tube in the vicinity of the air, just like that which is in the air-tight receptacles, remains fluid in part for two or three hours. In short, that my precautions in ensuring that these receptacles should be air-tight were, in so far as they applied to that object, utterly unnecessary. I mention this partly as an illustration of the deceptions to which one is liable in this inquiry, and partly because the experiment thus modified seems to tell as clearly against the ammonia theory as the original one seemed to tell in favour of it. Those receptacles which had been formed by the application of ligatures before the tube was opened afforded certainly no opportunity for the escape of ammonia, and yet in them the blood coagulated as quickly as in those which had communication with the air—implying that facility for the evolution of ammonia does not in itself affect the process of coagulation at all.

How then, it may be said, is the persistent fluidity of the blood under these circumstances to be explained? That will become more obvious than I can make it at present in the sequel; but in the mean time I may observe that there are probably two explanations :

one is, the coolness of the tube, and the other, far more important, that the blood, in slipping through this cylindrical tube, had had little opportunity of being influenced by its walls. The portion of the blood that came first in contact with the walls of the tube had coagulated; and it is to be observed that I never found, in these experiments, the blood altogether fluid, even after a comparatively short time: there has always been a certain amount of coagulation, and only a certain amount of fluidity. A layer of blood having thus coagulated upon the internal surface of the tube, the fresh blood which continued to flow through it, was not brought into contact with the walls of the tube at all, but with their lining of coagulated blood.

It has been long known that if blood is stirred with a rod, the process of coagulation is promoted. It seemed desirable to ascertain distinctly whether the cause of this was the contact of the foreign solid, or the opportunity given for the escape of ammonia; for it is quite true that, in the ordinary process of stirring blood, more or less air is mixed with it. For the purpose of determining this I devised a somewhat complicated experiment, which, however, it may be worth while to mention. I made an apparatus (fig. 2) of two portions of glass tube, A and B, connected in a vertical position by means of vulcanized india-rubber, I, the lower portion of the glass tube being also connected by india-rubber, I', with a wooden handle, H, which handle, H, was provided with an upright piece of wire, from which spokes projected in different directions, so

Fig. 2.



that they would, when moved, act as a churn on any blood contained in the lower portion of tube. When the lower piece of tube was fixed by means of a vice, V, the flexibility of the india-rubber permitted the churn to be rotated so as to expose the blood to its influence. This having been arranged, I first poured in strong *liquor ammonia*, so as to get rid of any slight acidity which the constituents of the apparatus might be conceived to possess, and then, having poured out the ammonia, filled up the apparatus with water, and boiled the whole in a large glass test-tube till all bubbles of air, in any portion of it, were expelled. Having then tied into a branch of the carotid artery, C, of a calf a bent tube of small diameter, as represented, and having permitted the blood to flow till it escaped at the orifice of the tube, I compressed the artery and passed the tube down through the water to the bottom of the apparatus, and then let the blood flow again, which had the effect of displacing all the water; and when the blood appeared at the top of the apparatus, the tube was withdrawn, when two effectual clamps, Cl, Cl, were placed on the vulcanized india-rubber connecting A and B; the india-rubber was then divided between the clamps, and we had the state of things represented at the right-hand side of the diagram. The upper portion of the apparatus, the orifice of which was exposed to the air, was set aside and left undisturbed. Having ascertained that the lower portion had been effectually sealed by the clamp, and thus prevented from any opportunity of escape of ammonia, I subjected it to the action of the churn for a certain number of minutes. It so happened that the blood of that calf was very slow in coagulating. I knew this from previous experiments on the animal, and therefore continued the action of the churn for a considerable time, viz. thirty-seven minutes. I then found the wire enveloped in a mass of clot; and examination of the fluid residue with a needle indicated that the fibrin had been all withdrawn from the blood on which the churn had acted. I did not now examine the other portion of the apparatus, which had been set aside; but at the end of an hour and a quarter, when more than double the time had elapsed, I investigated this, and found the blood in it, for the most part, still fluid and coagulable. Thus the blood in the churn, which, from the time it left the artery, had no oppor-

tunity of parting with its ammonia, coagulated much more rapidly than that in an open vessel. The difference between the two was, that the lower portion of the blood had been freely exposed to the influence of the foreign solid, whereas the other had only been subjected to the action of the wall of the tube.

The same principle may be illustrated by an exceedingly simple experiment which I performed only this very day. Receiving blood from the throat of a bullock into two similar wide-mouthed bottles, I immediately stirred one of them with a clean ivory rod for 10 seconds very gently, so as to avoid the introduction of any air, and then left both undisturbed. At the end of a certain number of minutes I found that, while the blood which had not been disturbed could be poured out as a fluid, with the exception of a thin layer of clot on the surface, and an incrustation on the interior of the vessel, the blood in the other vessel, which had been stirred for so brief a period, was already a solid mass.

I have only lately been aware of the great influence exerted upon the blood by exposure for a very short time to a foreign solid, and I feel that many of my own experiments, and many performed by others, have been vitiated for want of this knowledge. Take, for example, the effect of a vacuum, which was observed by Sir Charles Scudamore to promote coagulation. This has been considered by Dr. Richardson as an illustration of his theory, the vacuum being supposed to act by favouring the escape of ammonia. I have lately inquired into this subject, and I feel no doubt whatever that the greater rapidity of coagulation in a vacuum depends simply on the greater disturbance of the fluid. I made the following experiment :— I filled three bottles, such as these, from the throat of a bullock, placed one of them under the small bell jar of an air-pump in good order and exhausted it, leaving the other two undisturbed. The blood happened to be slow in coagulating ; and at the end of about forty minutes, in the vessels where the blood had been undisturbed, there was only a slight film of coagulum on the surface, whereas the blood under the vacuum was found on examination to have a very thick crust of clot upon it. But during the process of exhaustion the blood had bubbled very much. Indeed, any exhaustion of blood recently drawn which is sufficient to cause the evolution of its gases

induces great bubbling ; so that the pump cannot be used freely, for fear of the froth overflowing. To this disturbance, involving the exposure of successive portions of blood in the bubbles to the sides of the vessel, I was inclined to attribute the more rapid coagulation ; but in order to prove the point, I stirred for a few seconds the blood in one of the vessels hitherto undisturbed. After eight minutes I emptied the three vessels. I found that that blood which had not been disturbed at all, either by the vacuum or by the rod, was still almost entirely fluid, only showing a thin crust upon the glass and on the surface exposed to the air. The blood which had been subjected to the vacuum had a thick crust of clot on the surface, and the sides of the glass were also thickly encrusted, but it still contained a considerable quantity of fluid that could be poured out from its interior. But that blood which had been stirred for only a few seconds was a solid mass throughout. In other words, gentle stirring of the blood for a few seconds had much greater effect in producing coagulation than the protracted and efficient exhaustion which was continued for upwards of 40 minutes, which was a considerable time after all evolution of gas, as indicated by bubbles, had ceased.

Other experiments precisely similar in their effect were performed. I therefore feel no hesitation in stating that the effects of a vacuum, regarding which, indeed, the statements of different experimenters have hitherto been conflicting, afford no evidence in favour of the ammonia theory.

There is another point of very great interest in the history of the coagulation of the blood, which has been supposed to give support to the ammonia theory ; and that is, the effect of temperature. It has been long known that blood coagulates more rapidly at a high than at a low temperature, and, indeed, a little above the freezing-point remains entirely fluid. This seemed beautifully in harmony with the ammonia theory, as heat would naturally promote, and cold retard the evolution of the alkali, and a depression of temperature to near the freezing-point might be reasonably supposed to prevent its escape altogether. Indeed Dr. Richardson mentions as a fact, that ammonia artificially mixed with blood ceases to be given off under such circumstances.

Though thinking it not unlikely that this was the true explanation of the influence of temperature on coagulation, I thought it worth while to subject the matter to experiment. For that purpose I kept the blood of a horse fluid by means of a freezing-mixture, and afterwards by ice-cold water; and when the corpuscles had subsided from the upper part of the blood, I cautiously added to the liquor sanguinis extremely dilute ice-cold acetic acid till it was of distinctly acid reaction, the liquor sanguinis being of a colour that permitted the delicate application of test-paper, which is impossible with red blood. By this means any free ammonia which the fluid might have contained must have been neutralized; yet so long as it was kept in the cold it continued fluid, but when brought into a warm room, coagulated just as a specimen which had not been acidulated. Thus, when there could be no free ammonia in the liquor sanguinis at all, it was still affected as usual by temperature.

This experiment may not be satisfactory to all minds, though I confess it appears so to me; and as this is a point of very great interest, I have sought in another way for evidence regarding it. First, however, I will mention an experiment which will not at once appear to bear on the question of temperature. I drew out a fine glass tube in such a way as to produce a fusiform receptacle continued longitudinally each way into a tube of almost capillary fineness for about two inches, which again expanded at the end, as represented in fig. 3. Having squeezed out a drop of blood from my finger, I

Fig. 3.



sucked up a portion into the tube till the receptacle A and its capillary extensions were filled. I then broke off the expanded ends, and placed the little tube thus filled, B, in a bath of the strongest liquor ammoniæ. Here certainly the blood was in circumstances in which it could not lose ammonia, but where any change in its amount must be by way of increase, and yet I found, on opening the receptacle by

snapping it across after a scratch with a file, that instead of remaining longer fluid than in a watch-glass, the blood in it, being more in contact with the glass, was always more quickly coagulated, while coagulation was still more rapid in the capillary tube, where the blood was still more exposed to the influence of the foreign solid—the greater proximity to the liquor ammoniæ having no influence upon it.

It may perhaps be argued that the drop of blood employed being a small drop, and this small drop having been drawn up by suction into the tube, it might have parted with its ammonia before it got into the tube ; but then (and now comes the bearing of the experiment on the effect of temperature) I found, if I placed a similar tube filled in the same way in a vessel of snow, so as not to freeze it but to keep it ice-cold, the blood in it remained fluid as long as I chose to keep it there. Now if all the ammonia had left the blood before it was introduced into the tube, cold ought, according to the ammonia theory, to have had no effect in retarding its coagulation ; for, according to that theory, cold operates by retaining the ammonia. On the other hand, if we take the other alternative and suppose that any ammonia which the blood might have contained was still in these tubes, the former experiment proves clearly that the retention of ammonia has no effect in producing fluidity—no effect in preventing coagulation ; and if the retention of ammonia has no effect in preventing coagulation, then cold certainly cannot prevent coagulation by retaining the ammonia, because, even if retained, it would not influence the result. In whatever way we look at them, therefore, these simple experiments prove conclusively that cold maintains the fluidity of the blood in some manner unconnected with any influence it may exert upon ammonia.

Then, again, I varied the experiment in this way. I placed such little tubes of blood in baths of liquor ammoniæ at different temperatures. By careful management, guarding against the volatilization of ammonia and consequent reduction of temperature, I succeeded in employing satisfactorily a bath of liquor ammoniæ at 100° F., the blood being in the bath within a few seconds of its leaving the vessels of my finger, and I found that the high temperature, though under such circumstances it could not possibly dissipate any ammonia

from the blood, yet accelerated its coagulation in precisely the same way as when it was applied to blood in watch-glasses exposed to the air.

It is clear, then, that the promotion of the solidification of fibrin by heat is as independent of the evolution of ammonia as the coagulation of albumen under the same agency. Indeed it seems probable that the two cases are analogous, except that a higher temperature is required in the one than in the other.

When fine tubes containing blood were placed in liquor ammoniæ, the alkali acted only upon those parts which were close to the ends of the tubes; a very small portion was rendered brown by it, and beyond that a little was kept permanently fluid, but the chief length of the blood in the tube was unaffected. Having thus ascertained that ammonia travels so slowly along tubes of this capillary fineness, I thought I might have an opportunity of giving the ammonia theory a fair test by tying such a tube as has been above described into the jugular vein of a rabbit and filling it directly from the vessel, and then ascertaining whether there was any evidence of retardation of coagulation in the blood thus imprisoned. But I could discover no such evidence, although I sought for it in confirmation of a view I then held. To this, however, there is one special exception to be made, viz. in the case of asphyxia. I found that if two such tubes were filled from the same blood-vessel of a creature, one under normal circumstances, and the other after asphyxia had been induced, there was a most remarkable difference between the rates of coagulation of the blood in the two tubes, the asphyxial blood coagulating very much more slowly than the ordinary blood; but when the asphyxial blood was shed into a watch-glass and air was blown through it, it coagulated rapidly, showing that in the state of asphyxia there must be some volatile element in the blood which has an effect in retarding coagulation.

Supposing at first that this volatile element must be ammonia, I hoped to be able by chemical means to find evidence of its accumulation in asphyxia, and thus add a fact of great interest to physiology. Imitating experiments previously made by Dr. Richardson, I passed air successively through blood and through hydrochloric acid, and then estimated the amount of ammonia acquired by the latter by means of

oichloride of platinum. In order to prevent the possibility of the loss of any ammonia, I directed blood from the carotid artery of a calf fairly into a Woulfe's bottle by means of a vulcanized india-rubber tube tied into the vessel, and then drew a certain volume of air through it by means of an aspirating jar, the experiment being performed first before, and then during asphyxia. The same procedure was adopted with a second calf, the animal being in each case under chloroform, which does not interfere with the development during asphyxia of the peculiarity in the blood above alluded to; but I could not find satisfactory evidence of accumulation of ammonia; and without going further into the question at present, I may say that it seems much more probable that the effect is due to carbonic acid, which is known to have a retarding influence on coagulation, and which probably accumulates greatly in asphyxial blood.

But in justice to the author of the ammonia theory, and to myself, too, who at one time expressed a qualified belief in it, it is but fair to say that this theory is extremely plausible. It has been well shown by Dr. Richardson that ammonia is a substance well fitted to keep the blood fluid if it be present in a sufficient quantity. An experiment of my own illustrates very well the same point. I drew out a tube about a quarter of an inch in calibre (fig. 4), so that while

Fig. 4.



for two inches at one end it retained its original width, the rest (some ten inches) was pretty narrow, though far from having the capillary fineness of those before described. Into the thick part I introduced a drop of strong liquor ammoniæ, A, and then securely corked that end of the tube, C. The object of this was that there should be a strong ammoniacal atmosphere in the narrow part of the tube. I then opened a branch of a vein, V, in the neck of a sheep, introduced the narrow end of the tube into the vessel, and pushing it in so that its

orifice should be in the current of the main trunk of the vein, tied it in securely. I then removed the cork and made pressure on the vein at the cardiac side, causing the vessel to swell and blood to pass into the fine part of the tube ; and before the blood had reached the part of the glass moistened by the ammonia, I put in the cork again and withdrew the tube. In a short time, on introducing a hook of fine wire into the extremity of the tube, I found the blood already coagulated ; but on filing off a small portion of the tube, I found the blood there fluid. The portion of blood thus exposed soon coagulated, when, a second small piece of the tube being removed by the file, fluid blood was again disclosed, which again soon coagulated ; and this proceeding was repeated with the same results time after time, till, near the thick part of the tube, the ammonia in the blood was so strong as to prevent coagulation altogether.

This experiment illustrates how fitted the ammonia is to maintain the fluidity of blood, and also how apt it is, when present in the blood, to fly speedily off from it, leaving it unimpaired in its coagulating properties ; and it must be confessed that the end of the tube sealed with a small clot resembled most deceptively the extremity of a divided artery similarly closed. But although the experiment seems in so far to favour the ammonia theory, it will tell differently when I mention the object with which it was performed. It appeared to me that, if the cause of the fluidity of the blood was free ammonia, then, if I provided an ammoniacal atmosphere in the tube, and introduced blood by pressure directly from the vein into this ammoniacal atmosphere, this blood, lying between the strong ammoniacal atmosphere on the one side and the ammonia naturally present in the blood within the vein on the other side, ought to remain fluid ; and if it did remain fluid, this would tend to confirm the ammonia theory by making it appear that the volatile material was the same at both ends of the tube. But, to my disappointment, I invariably found that if I drew away the tube after a few minutes only had elapsed, there was already a clot in its extremity ; in other words, the ammonia had diffused from the end of the tube into the blood within the vein as into a non-ammoniacal atmosphere. This experiment alone, if duly considered, would, I think, suffice to show that the blood does not contain enough ammonia to account for its fluidity.

Fig. 5.

One more experiment, however, may be adduced with the same object. I mounted a short but wide glass tube, open at both ends (T, fig. 5), upon the end of a piece of strong wire, W, and connected with the latter a coil of fine silver wire, S, so that it hung freely in the tube. I then opened the carotid artery of a horse, and through the wound instantly thrust in the apparatus so far that I was sure the tube lay in the common carotid, which in veterinary language means the enormous trunk common to both sides of the neck of the animal. The tube being open at both ends, and slightly funnel-shaped at that end which was directed towards the heart, had thus a full current of arterial blood streaming through it. Having ascertained how long the arterial blood took to show the first appearance of coagulation in a watch-glass, I very soon after removed the apparatus, and, on taking out the coil of silver wire, found that it was already crusted over with coagulum. Yet here assuredly there had been no opportunity for the escape of ammonia.



From this experiment it is obvious that there is a very great difference between ordinary solid matter and the living vessels in their relation to the blood. But the same conclusion may be drawn much more simply from experiments which I had the opportunity of performing after making an observation which it seems strange should have been left for me to make, and which, I may say, was made by myself purely accidentally; and this is, that the blood of mammalia, although it coagulates soon after death in the heart and the principal arterial and venous trunks, remains fluid for an indefinite period in the small vessels. If, therefore, a ligature be tied round the foot of a living sheep a little below the joint which is divided by the butcher, the foot being removed and taken home with the blood retained in the veins by the ligature, we have a ready opportunity of investigating the subject of coagulation, and of making observations as satisfactory as they are simple. Here are two feet provided in the way I have alluded to. A superficial vein in each

foot has been exposed. The veins I see have contracted very much since I reflected the skin from them before our meeting; and I may remark that such contraction, dependent on muscular action, may occur days after amputation, indicating the persistence of vital properties in the veins. Now as I cut across this vein, blood flows out, fluid but coagulable. Into the vein of this other foot has been introduced a piece of fine silver wire, and when I slit up the vein you will see the effect it has produced. Exactly as far as the silver wire extends, so far is there a clot in this vessel. Now this experiment, very simple as it is, is of itself sufficient to prove the vital theory in the sense that the living vessels differ entirely from ordinary solids in their relation to the blood. It is perfectly clear that by introducing a clean piece of silver wire (and platinum or glass or any other substance chemically inert would have had the same effect) I do not add any chemical material or facilitate the escape of any, and yet coagulation occurs round about the foreign solid.

Again, if a blood-vessel be injured at any part, coagulation will occur at the seat of injury. As a good illustration of this, and also as bearing upon the ammonia theory, I may mention the following experiment. Having squeezed the blood out of a limited portion of one of the veins of a sheep's foot, and prevented its return by appropriate means, I treated the empty portion with caustic ammonia, the neighbouring parts of the vein being protected from the irritating vapour by lint steeped in olive oil. After the smell of ammonia had passed off, I let the blood flow back again and left it undisturbed for a while, when I found on examination a cylindriacal clot in the part that had been treated with ammonia, while in the adjacent parts of the same vessel the blood remained fluid. I repeated this experiment several times and always with the same result. Where the ammonia had acted there was a clot. The chemical agent used here was one which, so long as any of it remained, would keep the blood fluid; yet its ultimate effect was to induce coagulation, the vital properties of the vein having been destroyed by it.

If a needle or a piece of silver wire is introduced for a short time into one of the veins of the sheep's foot, it is found on withdrawal to be covered over with a very thin crust of fibrin, whereas the wall of the vessel itself is never found to have fibrin or coagulum adhering to it unless it has been injured. Now this seems to imply that the

ordinary solid is the active agent with reference to coagulation—that it is not that the blood is maintained fluid by any action of the living vessels, but that it is induced to coagulate by an attractive agency on the part of the foreign solid. We see at any rate that the foreign solid has an attraction for fibrin which the wall of the vessel has not.

And yet I own I was at first inclined to think that the blood-vessels must in some way actively prevent coagulation. There were two considerations that led to this view. One was, that the blood remained fluid in the small vessels after death, but coagulated in the large. Now why should that be? It seemed only susceptible of explanation from there being some connexion between the size of the vessel and the circumstance of coagulation. It looked as if in the small veins the action of the wall of the vessel was able to control the blood and keep it fluid, but that the large mass in the principal trunks could not be so kept under control. The other circumstance was, the rapid coagulation of a large quantity of blood shed into a basin. Why should this occur unless there was some spontaneous tendency in the blood to coagulate? It seemed scarcely credible that it was the result of contact with the surface of the basin.

Both these notions, however, have since been swept away. In the first place, I have observed recently that it is by no means only in small vessels that the blood remains fluid after death. If blood be retained within the jugular vein of a horse or ox by the application of ligatures, either before or after the animal has been struck with the poleaxe, it will often continue fluid, but coagulable, in that vessel, which is upwards of an inch in diameter, for twenty-four or even forty-eight hours after it has been removed from the body. I say often, but not always. The jugular vein seems to be in that intermediate condition, between the heart and the small vessels, in which it is uncertain whether it will retain its vital properties for many hours, or will lose them in the course of one hour or so. Unfortunately for my present purpose, it happens that in this jugular vein, removed from an ox six hours ago, coagulation has already commenced, as I can ascertain by squeezing the vessel between my fingers. But now that I lay open the vessel, you observe that the chief mass of its contained blood is still fluid, and we shall at all events have an opportunity of seeing that what is now fluid will in a short time be coagulated. It is an interesting

circumstance with reference to the question which we are now considering, that the coagulation always begins in contact with the vein, indicating that it is not the wall of the vessel that keeps the blood fluid, but that, on the contrary, the wall of the vessel, when deprived of vital properties, makes the blood coagulate.

The observation of the persistent fluidity of the blood in these large vessels furnished the opportunity of making a very satisfactory experiment, which I hoped to have exhibited before the Society; but as there was some clot in the vein, I did not think fit to run the risk of failure. The experiment is performed in the following way. A piece of steel wire is wound spirally round one of the veins in its turgid condition, and with a needle and thread the coats of the vessel are stitched here and there to the wire, care being taken to avoid puncturing the lining membrane, and thus the vessel is converted into a rigid cup. Two such cups being prepared, and the lining membrane of the vein being everted at the orifice of each so as to avoid contact of the blood with any injured tissue, I found that, after pouring blood to and fro through the air in a small stream from one venous receptacle into the other half a dozen times, and closing the orifice of the receptacle to prevent drying, the blood was still more or less completely fluid after the lapse of eight or ten hours. On the other hand, if a fine sewing-needle is pushed through the wall of an unopened vessel so that its end may lie in the blood, it is found on examination, after a certain time has elapsed, that the needle is surrounded with an encrusting clot. It is scarcely necessary to point out how entirely the ammonia theory and the oxygen theory, as well as that of rest, fail to account for facts like these.

While the blood may remain fluid for forty-eight hours in the jugular vein of a horse or an ox, it coagulates soon after death in the heart of very small animals, such as mice; so that it is obvious that the continuance of fluidity in small vessels is not due to their small size.

It is a very curious question, What is the cause of the blood remaining so much longer fluid in some vessels than in others? I believe that we must accept it simply as an ultimate fact, that just as the brain loses its vital properties earlier than the ganglia of the heart, so the heart and principal vascular trunks lose theirs sooner than the smaller vessels of the viscera, or than more superficial vessels, be they

large or small. We can see a final cause for this, so to speak. So long as the heart is acting, circulation will be sure to go on in the heart and principal trunks; whereas, on the contrary, the more superficial parts are liable to temporary causes of stagnation, and occasionally to what amounts to practical severance from vascular and nervous connexion with the rest of the body; and it is, so to speak, of great importance that the blood should not coagulate so speedily in the vessels of a limb thus circumstanced as it does in the heart after it has ceased to beat. Were it not for this provision, the surgeon would be unable to apply a tourniquet without fear of coagulation occurring in the vessels of the limb. As an illustration of the importance of a knowledge of these facts, I may mention a case that once occurred in my own practice. I was asked by a surgeon in a country district to amputate an arm which he despaired of. The brachial artery had been wounded, as well as veins and nerves, and at last, being foiled with the hemorrhage, he wound a long bandage round the limb at the seat of the wound as tightly as he possibly could. It had been in this condition with the bandage thus applied for forty-eight hours when I reached the patient; and the limb had all the appearance of being dead. It was perfectly cold, and any colour which it had was of a livid tint. But having been lately engaged in some of the experiments which I have been describing, and having thus become much impressed with the persistent vitality of the tissues and the concomitant fluidity of the blood, I determined to give the limb a chance by tying the brachial artery. Before I left the patient's house he had already a pulse at the wrist, and I afterwards had the satisfaction of hearing that the arm had proved a useful one.

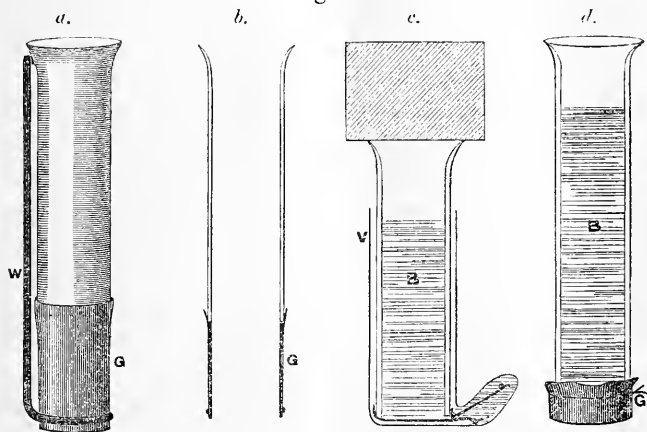
One of the two arguments in favour of activity on the part of the vessels as a cause of the fluidity of the blood having been completely disposed of, let us now consider the other, viz. the rapid coagulation of blood shed into a basin, appearing at first sight to imply a spontaneous tendency of the blood to coagulate, such as would have to be counteracted by the vessels. This also has proved fallacious.

In the first place it appears that the coagulation, after all, does not go on in a basin so suddenly as one would at first sight suppose, but always commences in contact with the foreign solid. When blood has been shed into a glass jar, if, on the first appearance of a film at the surface, you introduce a mounted needle curved at the end be-

tween the blood and the side of the glass and make a slight rotatory movement of the handle, you see through the glass the point of the needle detaching a layer of clot whatever part you may examine. The process of coagulation having thus commenced in contact with the surface of the vessel into which the blood is shed, may under favourable circumstances be ascertained to travel inwards, like advancing crystallization, towards the centre of the mass. It appears, however, that this extension of the coagulating process would not take place had not the blood been prepared for the change by contact, during the process of shedding, with the injured orifice of the blood-vessel and with the surface of the receptacle. I have only very recently become acquainted with the remarkable subtlety of the influence exerted upon blood by ordinary solids. I was long since struck with the fact, that if I introduced the point of an ordinary sewing-needle through the wall of a vein in a sheep's foot and left it for twelve hours undisturbed, the clot was still confined to a crust round the point of the needle, implying that coagululum has only a very limited power of extension. I thought, therefore, that by proper management it might be possible to keep blood fluid in a vessel of ordinary solid matter lined with clot. But various attempts made with this object failed entirely, till I lately adopted the following expedient. Having opened the distal end of an ox's jugular vein containing blood and held in the vertical position, taking care to avoid contact of any of the blood with the wounded edge of the vessel, I slipped steadily down into it a cylindrical tube of thin glass, somewhat smaller in diameter than the vein, open at both ends, and with the lower edge ground smooth in order that it might pass readily over the lining membrane, and so disturb the blood as little as possible by its introduction, and influence only the circumferential parts of its contents. The tube was then kept pressed down vertically upon the bottom of the vein by a weight, in a room as free as possible from vibration, and I found on examining it at the end of twelve hours that the clot was a tubular one, consisting of a crust about one-eighth of an inch thick next the glass and the part exposed to the air, but containing in its interior fluid and rapidly coagulable blood. In another such experiment, continued for twenty-fours, though the crust of clot was thicker, the central part still furnished coagulable blood.

But it may perhaps be argued by those who say that the blood-vessels are active in maintaining fluidity, that the small portion of the vein covering the end of the tube was acting upon the blood, which certainly was fluid where in contact with it, the clot being in the form of a tube open at the lower end. To guard against such an objection I made the following experiment:—I extended a tube like that above described by means of thin sheet gutta percha, G (fig. 6*a*),

Fig. 6.



contriving that the internal surface of the gutta percha should be perfectly continuous with that of the glass tube as represented in section in fig. 6*b*. The lower part of the gutta-percha tissue was strengthened by a ring of soft flexible wire such as is used by veterinary surgeons for sutures, and the wire W was also extended upwards to the top of the glass so as to maintain the rigidity of the gutta-percha portion during its introduction into a vein, but at the same time, from its softness, permit the gutta-percha part to be bent at a right angle after it had been introduced, and so close the orifice of the glass tube with ordinary solid matter. In fig. 6*c* the tube is represented pressed down by a weight in a vein V, with blood B in the glass portion, while the gutta-percha part closes it below. At the same time I performed a comparative experiment, to which I would invite particular attention, although I am sorry at this late hour to occupy the attention of the Society so long. I tied a thin piece of gutta-percha tissue over the lower end of a similar glass tube, and simply

poured blood into it from the jugular vein of an ox. I wished to compare the condition of blood which had been simply poured into a tube, with blood which had been introduced without any disturbance of its central parts. But in order to make the experiment a fair one, as it might be said that the blood poured from the vein had been more exposed to the air than that into which the tube was slipped, I proceeded in the following way:—I obtained a long vein containing plenty of blood, and having first filled the second tube, with the gutta-percha bottom (fig. 6 *d*), by simply pouring blood into it from the vein, I cut off a portion of the vein which had been thus emptied, and having tied one end and everted the lining membrane of the other end, and having also everted the lining membrane of the orifice of the remainder of the vessel which was full, I poured the blood from the full portion through the air into the empty part. In doing this I had difficulty in getting blood enough, and it passed through the air in slow drops, and that only when the vein was squeezed by my warm hand. At last, having introduced sufficient for the purpose, I slipped down the compound tube and bent its gutta-percha portion, as represented in fig. 6 *c*, and left both tubes for a while undisturbed. At the end of three hours and a half I found that the blood which had been simply poured in was a mass of clot, and fluid squeezed from it yielded no threads of fibrin, coagulation being complete. How long it had been so I do not know. I did not examine the other blood until seven hours and three quarters had expired, and then found that, just as in the cases where a simple glass tube was introduced, the clot was tubular, and the chief part of the blood was still fluid in its interior, the only difference being that in this case the clot formed a complete capsule, being continued over the gutta percha instead of being deficient below, as it was when the vein closed the end of the tube. Now if we consider the two parts of this comparative experiment, we see that the receptacles in which the blood was ultimately contained were precisely similar in the two cases, viz. glass tubes closed below with gutta percha; and that the blood which was simply poured into the tube was much less exposed to the air than the other, and also was not subjected, like it, to elevation of temperature, a circumstance which promotes coagulation; but yet this blood became completely coagulated in a comparatively short time, whereas the other after a much

longer time was coagulated only in a layer in contact with the foreign solid. But in the latter case the blood had been so introduced as to avoid direct action of ordinary matter on any but the circumferential parts of it; whereas in the former, though poured quickly, it had run down the side of the glass, and as a consequence of this almost momentary contact with the foreign solid, the central parts, like the circumferential, underwent the process of coagulation.

Mysterious as this subtle agency of ordinary solids must appear, its occurrence is thus matter of experimental demonstration, and by it the coagulation of blood shed into a basin is accounted for; while it is also shown conclusively from this experiment that the blood, as it exists within the vessels, has no spontaneous tendency to coagulate, and therefore that the notion of any action on the part of the blood-vessels to prevent coagulation is entirely out of the question. The peculiarity of the living vessels consists not in any such action upon the blood, but in the circumstance, remarkable indeed as it is, that their lining membrane, when in a state of health, is entirely negative in its relation to coagulation, and fails to cause that molecular disturbance or, if we may so speak, catalytic action which is produced upon the blood by all ordinary matter.

I afterwards found that the simplest method of maintaining blood fluid in a vessel composed entirely of ordinary matter was to employ a glass tube similar to those above described, except that its upper end was closed by a cork perforated by a narrow tube terminating in a piece of vulcanized india-rubber tubing that could be closed by a clamp. This tube was slipped down into a vein till the blood, having filled it completely, showed itself at the orifice of the india-rubber tubing, to which the clamp was then applied. The whole apparatus was now quickly inverted, and the vein was drawn off from over the mouth of the tube, which was then covered with gutta-percha tissue to prevent evaporation. After the inverted tube had been kept undisturbed in the vertical position for nineteen hours and three quarters, coagulable blood was obtained from the interior of the clot.

We have seen that a clot has but very slight tendency to induce coagulation in its vicinity unless the blood has been acted on by an ordinary solid; and it is probable that with perfectly healthy blood

it would be unable to produce such an effect at all. This appears to me to be very interesting physiologically, but especially so with reference to pathology. I must not go now fully into the circumstances that lead me to it ; but I may express the opinion I have formed, that clot must be regarded as living tissue in its relation to the blood. It is no doubt a very peculiar form of tissue, in this respect, that it is soft, easily lacerable, and easily impaired in its vital properties. If disturbed, as in an aneurism, it will readily be brought into that condition which leads to the deposition of more clot ; but if undisturbed, it not only fails to induce further coagulation, but seems to undergo spontaneous organization. I have seen a clot in the right side of the heart, and extending into the pulmonary artery and its branches, unconnected with the lining membrane of auricle or ventricle or with the pulmonary artery except at one small spot where it had a slight adhesion, developed into perfect fibrous tissue by virtue, it would appear, of its own inherent properties. Another observation which I once made, and which then completely puzzled me, now seems capable of explanation. In laying open the blood-vessels of a dead body, I observed in many of the veins a delicate white lace-like tissue which evidently must have been formed from a clot. This I now believe to have had the same relation to the coagulum as the flimsy cellular tissue of old adhesions has to lymph.

It may not be altogether superfluous to mention some other facts illustrative of the active influence of ordinary matter in promoting coagulation, and the negative character of the lining membrane of the vessels. I find that a needle introduced into one of the veins of the foot of a sheep for a much shorter time than is necessary to produce the first appearance of the actual deposit of fibrin upon it, leads after a while to coagulation where the needle had lain—in other words, that a foreign solid, by a short period of action on the blood, brings about a change that results in coagulation, though the blood still lies in the living vessels. I have also ascertained that after blood has been made to coagulate in a particular vessel by introducing a needle into it, if the coagulum as well as needle is removed, and more fluid blood is allowed to pass in, this blood remains fluid for an indefinite period, showing that the needle had not impaired the properties of the vessel by its presence ; so that the previous coagulation

must be attributed not to any loss of power in the vein, but simply to the action of the foreign solid.

In seeking for an analogy to this remarkable effect of ordinary solids upon the blood, we are naturally led to the beautiful observations of Professor Graham, lately published in the *Philosophical Transactions*. He has there shown what insignificant causes are often sufficient to induce a change from the fluid or soluble to the “pectous,” or insoluble condition of “colloidal” forms of matter. Indeed Mr. Graham has himself alluded to the coagulation of fibrin as being probably an example of such a transition.

There is, however, another remarkable circumstance that must be taken into consideration, of which I myself have been only recently aware, and which may be new to several Fellows of the Society; and that is, that in spite of the influence of an ordinary solid the liquor sanguinis is not capable of coagulating *per se*. It was observed many years ago by my colleague, Professor Andrew Buchanan, of Glasgow, that the fluid of a hydrocele, generally regarded as mere serum, coagulated firmly if a little coagulum of blood diffused in water was added to it—an effect which he was disposed to attribute to the agency of the white corpuscles*. I repeated Dr. Andrew Buchanan’s observations last year, and satisfied myself first that the diffused clot did not act simply by providing solid particles to serve as starting-points for the coagulating process. I tried various different materials in a finely divided state, and found that none of them, except blood, produced the slightest effect. But I found that if a mixture of serum and red corpuscles from a clot was added to some of this hydrocele-fluid, it was soon converted into a firm solid mass. If a small quantity of the serum and corpuscles was dropped into the fluid and allowed to subside without stirring, coagulation rapidly took place in those parts where the red corpuscles lay, while other parts of the fluid remained for a long time uncoagulated. This seemed to indicate that the red corpuscles had a special virtue in inducing the change. I confess, however, that till very lately I was inclined to suppose that in the hydrocele-fluid the fibrin must be in some peculiar spurious form. We know that the buffy coat of the horse’s blood coagulates in a glass without addition of clot, and we know that lymph coagulates; so that I did not doubt

* Proceedings of the Glasgow Philosophical Society, February 19, 1845.

that liquor sanguinis would always undergo the change when influenced by ordinary matter. But an observation which I made not many days ago, shows that this was a mistake. I obtained the jugular vein of a horse, and having kept it for a while in a vertical position till I could see through its transparent coats that the red corpuscles had fallen from the upper part, I removed all bloody tissue from that part of the vein, and punctured it so as to let out the liquor sanguinis into a glass. Finding after eighteen minutes that the liquid had not begun to coagulate, I added a drop of serum and corpuscles to a portion of it, and within seven minutes there was a clot wherever the corpuscles lay, whereas the rest of the fluid was still very imperfectly coagulated after another half hour had elapsed. That the liquor sanguinis to which no addition had been made coagulated at all, was sufficiently explained by microscopic investigation, which showed not only abundant white corpuscles, but also several isolated red ones that had not subsided. This observation was made three hours after the death of the horse, but I obtained essentially similar results on repeating the experiment in another horse an hour after death; so that there can be no doubt whatever that the fibrin was in the same condition as it is in the blood-vessels of a living animal. The observation appears also particularly satisfactory on this account, that the liquor sanguinis was not separated from the corpuscles by any process of transudation through the walls of the blood-vessels, which might be conceived to involve retention of some constituent of the liquid, which, though in solution, might be unable to pass through their pores, but simply by the subsidence of the corpuscles, which must have left all the materials of the liquor sanguinis behind them. Hence it is proved beyond question that if the liquor sanguinis could be separated completely from the blood-corpuscles, it would resemble the fluid of hydrocele in being incapable of coagulation when shed into a cup.

Now this struck me as a very satisfactory and beautiful truth, inasmuch as it clears away all the old mystery of the distinction between inflammatory exudations and dropsical effusions. Dropsical effusions, exhibiting little disposition to coagulate, have been supposed to consist almost exclusively of serum, and the exudation of the entire liquor sanguinis has been regarded as the special characteristic of inflammation; and very unsatisfactory theories have been

put forward by ingenious pathologists to account for this difference. But it now appears that a dropsical effusion, like that of hydrocele, is undistinguishable from pure liquor sanguinis.

Various dropsical effusions have been lately investigated with reference to their coagulability on the addition of blood-corpuscles, by Dr. Schmidt of Dorpat, who finds that while they differ from one another in the amount of water they contain (just as is the case with serum filtered artificially through animal membranes under different degrees of pressure), yet they are all but universally coagulable. Schmidt has also carried the investigation further. He has found that by chemical means he can extract from the red corpuscles a soluble material which, when added to these exudations, leads to coagulation. In other words, he shows that the corpuscles do not act as living cells, but by virtue of a chemical material which they contain, which can be used in the state of solution, free from any solid particles whatever. He found also that the aqueous humour made a dropsical effusion coagulate, and that the same effect was produced by a material extracted from the non-vascular part of the cornea. Hence he regards the blood-corpuscles as only resembling other forms of tissue in possessing this property. These observations are extremely interesting, if trustworthy; and that they are so, I do not at all doubt; but having only read Schmidt's papers within the last day or two, I have not yet had opportunity of verifying his statements*.

It remains to be ascertained what share the material derived from the corpuscles has in the composition of the fibrin. Schmidt inclines to the opinion that the fibrin is probably composed, in about equal proportions, of a substance furnished by them and one present in the liquor sanguinis. If this be true, the action of an ordinary solid in determining the union of the components of the fibrin may be compared to the operation of spongy platinum in promoting the combination of oxygen and hydrogen.

* Since this lecture was delivered I have verified an important observation made by Schmidt, viz. that a given amount of corpuscles causes complete coagulation of only a limited quantity of hydrocele-fluid. From this he draws the inference, that the action of the corpuscles cannot be of the nature of fermentation—the coagulative efficacy of the corpuscles being not continued indefinitely, but becoming exhausted in the process of coagulation. For Schmidt's papers, see *Archiv für Anat. Phys. &c.* 1861 and 1862.

It may be asked, How comes it that when the blood of a horse is shed into a cup, the buffy layer coagulates as rapidly, or nearly so, as the lower parts rich in corpuscles?

This is indeed a question well worthy of careful study. We know that the liquor sanguinis left by the subsidence of the red corpuscles within a healthy vein is incapable of coagulating when shed, except in a slow manner, which is accounted for by the corpuscles that remain behind in it. Hence it appears that when the blood as a whole is shed into a glass, the agency of the ordinary solid leads the corpuscles to communicate to the liquor sanguinis, before they subside, a material or at least an influence which confers upon it a disposition to coagulate, though it still remains fluid for some time after they have left it. Just as we have seen that a very short time of action of the ordinary solid upon the blood as a whole is sufficient to give rise to coagulation, so we now see that, provided an ordinary solid be in operation, the presence of the corpuscles for but a little while is enough to make the liquor sanguinis spontaneously coagulable, though not immediately solidified. We shall see, before concluding, an illustration of the importance of this fact to pathology.

It remains to be added, that serous membranes resemble the lining membrane of the blood-vessels in their relations to the blood, as is implied by John Hunter's observation that blood, which had lain for several days in a hydrocele, coagulated when let out. The same thing is well illustrated in a frog prepared like this which I now exhibit. About four hours ago, a knife having been passed between the brain and cord to deprive the creature of voluntary motion in the limbs and trunk, the peritoneal cavity was laid open in the middle line, and its edges being kept raised and drawn aside by pins, I seized the apex of the ventricle of the heart with forceps and removed it with scissors. In a short time the whole of the animal's blood was in the peritoneum, and it may be seen that it is still fluid in spite of this long-continued exposure. When I first performed the experiment three years and a half ago, the weather being cool (about 45° Fahr.) and a piece of damp lint being kept suspended above the frog to prevent evaporation and access of dust, I found that the blood remained fluid in the peritoneal cavity for four days, except a thin film on the surface, and a crust of clot on the wounded part of the heart; but a piece of clean glass placed in the blood in the

peritoneum became speedily coated with coagulum. Here, it will be observed, not merely the liquor sanguinis, but the corpuscles also were present in the serous cavity, yet no coagulation took place in contact with its walls.

I think it probable, though not yet proved, that all living tissues have these properties with reference to the blood. We know that the interstices of the cellular tissue contain coagulable fluid, and I have seen anasarcaous liquid coagulate after emission ; but this indeed may possibly have been merely liquor sanguinis, coagulating in consequence of slight admixture of blood-corpuscles from the wounds made in obtaining it.

Looking now at the principal results which we have arrived at, it must, in the first place, be admitted that the ammonia theory is to be discarded as entirely fallacious. The fact that this theory is exceedingly plausible, and has been supported by many ingenious arguments and experiments, is of course no reason why we should retain it if unsound. On the contrary, the more specious it is the more necessary is it that it should be effectually cleared away ; for it mystifies the subject of coagulation most seriously ; and I may say, for my own part, that it has cost me an amount of experimental labour of which the illustrations brought forward this evening convey but little idea. Still these have been, I trust, sufficient to show that the coagulation of the blood is in no degree connected with the evolution of ammonia, any more than with the influence of oxygen or of rest. The real cause of the coagulation of the blood, when shed from the body, is the influence exerted upon it by ordinary matter, the contact of which for a very brief period effects a change in the blood, inducing a mutual reaction between its solid and fluid constituents, in which the corpuscles impart to the liquor sanguinis a disposition to coagulate. This reaction is probably simply chemical in its nature ; yet its product, the fibrin, when mixed with blood-corpuscles in the form of an undisturbed coagulum, resembles healthy living tissues in being incapable of that catalytic action upon the blood which is effected by all ordinary solids, and also by the tissues themselves when deprived of their vital properties.

These principles have, of course, very extensive applications to the study of disease ; but I must content myself with alluding very

briefly to inflammation, the most important of all pathological conditions.

If we inquire what is the great peculiarity of inflamed parts in relation to the blood as examined by the naked eye, we see that it consists in a tendency to induce coagulation in their vicinity—implying, according to the conclusions just stated, that the affected tissues have lost for the time being their vital properties, and comport themselves like ordinary solids. Thus, when an artery or vein is inflamed, coagulation occurs upon its interior, in spite of the current of blood, precisely as would take place if it had been artificially deprived of its vital properties. On one occasion I simulated the characteristic adherent clot of Phlebitis by treating the jugular vein of a living sheep with caustic ammonia, and then allowing the circulation to go on through the vessel for a while, when, on slitting it up, I found its lining membrane studded with grains of pink fibrin which could be detached only by scraping firmly with the edge of a knife. Again, comparing an inflammatory exudation into the pericardium or into the interstices of the cellular tissue with dropsical effusions into the same situations, we are struck with the fact that, while the liquor sanguinis effused in dropsy remains fluid, the inflammatory product coagulates. Now we know that in intense inflammation the capillaries are choked more or less with accumulated blood-corpuscles, which must cause great increase in the pressure of the blood upon their walls; and from what we know of the effect of venous obstruction in causing dropsical effusion of liquor sanguinis through increased pressure, we are sure that we have in the inflammatory state the physical conditions for a similar transudation of fluid through the walls of the capillaries. And the natural interpretation of the difference in the two cases as regards coagulation seems to be, that whereas in dropsy the fluid is forced through the pores of healthy vessels, in inflammation the capillary parietes have lost their healthy condition, and act like ordinary matter; so that the liquor sanguinis, having been subjected, immediately before effusion, to the combined influence of the injured tissue and the blood-corpuscles, has acquired a disposition to coagulate, just like the buffy coat of horses' blood shed into a glass, or like the frog's liquor sanguinis filtered by Müller from its corpuscles, the injured vessels acting upon the blood like the filter.

This view of the condition of intensely inflamed parts is exactly that to which I was led some years ago by a microscopic investigation, the results of which were detailed in a paper* that received the honour of a place in the Philosophical Transactions. It was there shown, as I think I may venture to say, that the tissues generally are capable of being reduced under the action of irritants to a state quite distinct from death, but in which they are nevertheless temporarily deprived of all vital power, and that inflammatory congestion is due to the blood-corpuscles acquiring adhesiveness such as they have outside the body, in consequence of the irritated tissues acting towards them like ordinary solids.

I cannot avoid expressing my satisfaction that this inquiry into the coagulation of the blood has furnished independent confirmation of my previous conclusions regarding the nature of inflammation.







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